

IRB Review of Adverse Events



PENN's Response to Managing Adverse Event Reports

Yvonne K. Higgins, CIP
Associate Director
Office of Regulatory Affairs
University of Pennsylvania

IRB Review of Adverse Events Reports

Purpose of IRB Review

- Determine that the risk-benefit ratio continues to be acceptable
- Determine whether the informed consent document requires revisions
- Determine whether subjects currently enrolled need to be re-consented

“All IRBs recognize and acknowledge this responsibility, but few IRBs are equipped to handle the avalanche of AE reports sent by sponsors via the investigator.” Ernest Prentice, et.al., *IRB Management and Function*



PENN Statistics

- PENN receives >250 individual safety reports each week (approximately 13,000 reports each year from industry sponsors (through the PENN Principal Investigator)
- For multi-center industry sponsored clinical trials, the sponsor provides insufficient data in the form of individual safety reports that provide no meaningful context for analyzing individual reports
 - Randomization to test or placebo group may be blinded
 - No denominator



PENN's Perspective

The sponsor, data safety & monitoring board, & investigator are best positioned to assess individual safety reports. This position is supported by the regulations.

- 21 CFR 312.32(c)(1)(a): The sponsor shall notify the FDA and participating investigators of any adverse experience associated with the use of a drug that is both serious, and unexpected.
- 21 CFR 56.108(b)(1): Institutional responsibility to ensure prompt reporting of “any unanticipated problems posing risks to subjects or others



Individual IND Safety Reports

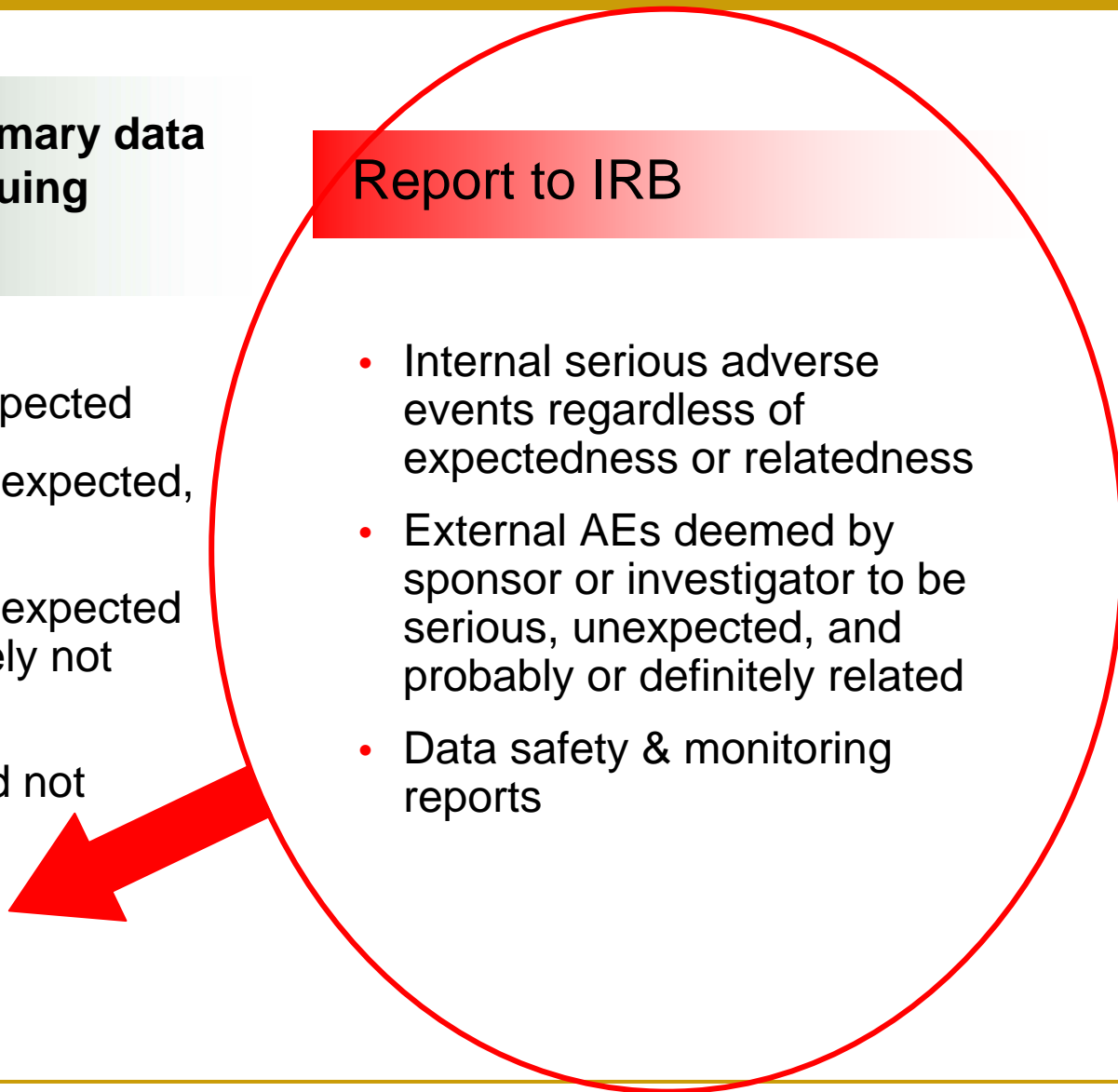
**Provide IRB with summary data
at the time of continuing
review**

- External, serious, expected
- External, serious, unexpected, unrelated
- External, serious, unexpected & possibly or definitely not related
- Internal AEs deemed not serious

Report to IRB

- Internal serious adverse events regardless of expectedness or relatedness
- External AEs deemed by sponsor or investigator to be serious, unexpected, and probably or definitely related
- Data safety & monitoring reports

***Promptly
INFORM IRB***



PENN AE Reporting System

- Provide a central repository of adverse events information that includes historical and current data.
- Provide the ability to create Notice to Sponsor reports
- Makes the data easily accessible via any web browser
- Provides a tool to monitor and maintain information in a consistent/easily auditable manner
- Facilitate annual reporting
- Provide an immediate date/time stamped electronic report to the Office of Regulatory Affairs




Penn AE System

ORA Adverse Events - Login - Netscape 6

File Edit View Search Go Bookmarks Tasks Help

https://rosetta.upenn.edu/cgi-bin/websec/websec_authform?app=pennaes&websec_page=https://pennaes... Search

Home My Netscape Search Shop Bookmarks Net2Phone

 **Penn Office of Regulatory Affairs**

Log into Adverse Events system

Please note that you will need a **valid PennKey** in order to access this application.

For more information please visit the [PennKey](#) website

PennKey:

Password:

Login

Office of Regulatory Affairs, 133 S. 36th Street, Mezzanine Floor, Philadelphia, PA 19104-3246

- Create AE record
- Find an existing AE record
- Create summary of AEs associate with a protocol
- Report AE to the Office of Regulatory Affairs
- Print out date stamped AE report

Document: Done (2.183 secs)

Start | Eudora | meetingm... | Office of ... | Norton A... | Microsoft ... | Microsoft ... | ORA Adv... | 11:06 AM



Penn AE Report

ORA Adverse Events - Adverse Events - Netscape

 **Penn Office of Regulatory Affairs** 

[Online Help](#)

Adverse Events

[Return to main page](#)

Protocol #706173, PI PennCard #10080362, Results sorted by Protocol, Event Date, Report Date.

Results 1-10 of 54 (per page)

Adverse Event ID: 5011	Patient Status: Randomized	Serious: No	Patient ID: 456489113
Principal Investigator: 10080362	Event Date: 09/12/2002	On Site: Yes	Outcome: Resolved
Protocol Number: 706173	Report Date: 09/12/2002	Age: 24	Event Category: Product problem
Sponsor: In House Project	Report Type: Initial	DOB: N/A	Serious Event Type: Other
Protocol Description: This is a test protocol for display purp ...	Informed Consent?: Yes	Sex: Female	Study Related: Unlikely to be Related
Event Severity: Category 1 = Mild	Amend Consent: No	Race: Native Hawaiian or Pacific Islander	
Event Description: complete required information to get to page 2			
Complete Description: final required field			

Adverse Event ID: 5009	Patient Status: Screening	Serious: No	Patient ID: 4564613
Principal Investigator: 10080362	Event Date: 09/02/2002	On Site: Yes	Outcome: Resolved
Protocol Number: 706173	Report Date: 09/05/2002	Age: 56	Event Category: Product problem
Sponsor: In House Project	Report Type: Initial	DOB: N/A	Serious Event Type: Other
Protocol Description: This is a test protocol for display purp ...	Informed Consent?: No	Sex: Male	Study Related: Not Related
Event Severity: Category 1 = Mild	Amend Consent: No	Race: Hispanic/Latino	
Event Description: fdagawegfawegf			
Complete Description: fdasgrwarfdsgatewatrgahsdftgrew			

Document: Done



Recommendation to FDA

Consistent with the regulations at 21 CFR, provide clear guidance to industry sponsors on the regulatory requirement to report to the IRB (through the investigator) unanticipated problems that pose risks to subjects or others.

- The sponsor is responsible for assessing adverse events and for providing meaningful, clear, and complete data to assist the IRB in meeting its regulatory and ethical obligations.
 - *Summary reports*
 - *DSMB reports*

